



Overview of Cirrhosis

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What is cirrhosis?

- **End-stage** of chronic liver disease
- Characterized by **advanced fibrosis/scarring**
- Complications include portal hypertension, varices, ascites, HE, HRS, SBP, liver cancer, and liver failure
- Common causes: alcohol-associated liver disease, chronic viral hepatitis infection, nonalcoholic fatty liver disease
- Diagnosed by **liver biopsy** (gold standard but invasive) or clinical findings (imaging, labs, medical history, presentations)



Classification of cirrhosis

- Child-Turcotte-Pugh (**CTP**) or Child-Pugh (**CP**) score assesses stage and severity of cirrhosis
 - Considers total bilirubin, albumin, INR, and degree of ascites and encephalopathy
 - Classifies into A (compensated), B (early decompensated), or C (severely decompensated)
- Model for End-Stage Liver Disease (**MELD**) score assesses prognosis (3-month mortality) for patients with cirrhosis
 - 12 or higher predicts increased risk of complications



Goals of therapy

- Prevent complications of cirrhosis
- Prevent hepatic decompensation
- Reduce mortality

Cirrhosis

Scarring/fibrosis leads to increased hepatic resistance

Portal Hypertension

Redirection of blood flow to collateral veins

Varices

Splanchnic vasodilation

Activation of endogenous vasoconstrictive systems (e.g., RAAS)

Renal vasoconstriction and sodium retention

Ascites

Hepatorenal Syndrome

Hepatic dysfunction leads to increase in systemic ammonia

Hepatic Encephalopathy

Bacterial translocation

Spontaneous Bacterial Peritonitis

HE Hepatic encephalopathy

HRS Hepatorenal syndrome

SBP Spontaneous bacterial peritonitis



Portal Hypertension (PH) & Varices

- Scarring of liver impedes blood flow through portal vein, increasing the blood pressure
 - **Varices** = distension in collateral vessels from redirected blood; at risk of **variceal hemorrhage**
- PH defined as **hepatic venous pressure gradient (HVPG) > 5 mmHg**
 - HVPG = difference in pressure between portal vein and hepatic veins
 - HVPG $\geq$ 10 mmHg = **clinically significant portal hypertension (CSPH)**
- **Primary prophylaxis of variceal hemorrhage**
 - A beta-blocker (**propranolol** 20-40 mg twice daily, **nadolol** 20-40 mg once daily, or **carvedilol** 6.25 mg twice daily) continued indefinitely, **OR**
 - Endoscopic variceal ligation (**EVL**) every 2-8 weeks until variceal eradication
- **Treatment of acute variceal hemorrhage**
 - **IV ceftriaxone** (1 g/day x max 7 days) + **EVL** + a vasoactive drug (see below)
 - **Octreotide**: 50 mcg bolus $\rightarrow$ continuous infusion at 50 mcg/hr for 2-5 days, **or**
 - **Vasopressin**: continuous infusion at 0.2-0.4 units/min (max 0.8 units/min) for 24 hours + concurrent IV nitroglycerin to maintain SBP of 90 mmHg, **or**
 - **Terlipressin**: 2 mg IV every 4 hours during the first 48 hours to control bleeding, then 1 mg every 4 hours to prevent rebleeding (total duration 2-5 days)
- **Secondary prophylaxis of variceal hemorrhage**
 - A non-selective beta-blocker (**propranolol** 20-40 mg twice daily or **nadolol** 20-40 mg once daily) continued indefinitely, **AND**
 - **EVL** every 1-4 weeks until variceal eradication



Spontaneous Bacterial Peritonitis (SBP)

- Often no clear source of infection; mainly Gram-negative bacteria (*E. coli*, *K. pneumoniae*) but some Gram-positive organisms can be common (*S. aureus*, *E. faecalis*, *E. faecium*)
- **Diagnosis**: polymorphonuclear (PMN) leukocyte > 250/mm³ in the ascitic fluid
- **Treatment: antibiotic therapy + IV albumin**
 - Empiric 3rd-gen cephalosporin (e.g., **ceftriaxone**, **cefotaxime**) generally recommended
 - **Broad spectrum** agents (e.g., **piperacillin/tazobactam**) recommended for healthcare-associated or nosocomial infection, those with recent exposure to broad-spectrum abx, or those admitted with sepsis/septic shock
 - Add **vancomycin** if prior MRSA infection or positive MRSA swab
 - Add **daptomycin** for vancomycin-resistant enterococcus
 - **Meropenem** +/- glycopeptide if current or recent exposure to piperacillin/tazobactam
 - Repeat diagnostic paracentesis **48 hours** from initiation; PMN decrease of **< 25%** from baseline may require broadening of antibiotic therapy or investigation of secondary peritonitis
- **Secondary prevention**
 - Long-term prophylaxis with **ciprofloxacin** 500 mg/day
- **Primary prevention**
 - IV ceftriaxone for patients with variceal hemorrhage (see PH & Varices section)
 - Generally only needed if high risk of infection present
 - **Ciprofloxacin** for patients with low ascitic fluid protein (< 1.5 g/dL) + and renal dysfunction or liver failure



Ascites

- Accumulation of **excess fluid** in the abdomen; often the first decompensating event
- **Dietary sodium restriction (to 2 g/day)** recommended for net fluid loss
- **Diuretic therapy (aldosterone antagonist + loop diuretic)**
 - **Preferred**: spironolactone + furosemide
 - Initially **spironolactone 100 mg + furosemide 40 mg per day**
 - Titrate to maximum of spironolactone 400 mg + furosemide 160 mg per day
 - At least **72-hour interval** needed between dose titrations
 - Taper down to the lowest effective dose after fluid is adequately mobilized
- Monitor daily body weight to assess efficacy of diuretics
 - Up to **0.5 kg/day weight loss** is generally appropriate (up to 1 kg/day for those with edema)



Hepatorenal Syndrome (HRS)

- Renal complication due to hemodynamic changes and systemic inflammation associated with cirrhosis
- **Diagnosis of HRS-AKI (acute kidney injury from HRS)**
 - Cirrhosis with ascites
 - Diagnosis of AKI ($\uparrow$ SCr by $\geq$ 0.3 mg/dL in 48 hr OR $\geq$ 50% $\uparrow$ in SCr in the past 7 days)
 - No response after 2 consecutive days of diuretic withdrawal & plasma volume expansion with albumin infusion
 - No current/recent use of nephrotoxic drugs, structural kidney injury, or shock
- **Treatment of HRS-AKI**
 - Vasoconstrictor (**terlipressin** preferred; **norepinephrine** also recommended) + **albumin**
 - Decrease in SCr to < 1.5 mg/dL or return to baseline within 0.3 mg/dL over maximum of **14 days** indicates **successful response**



Hepatic Encephalopathy (HE)

- Believed to be due to ammonia accumulation caused by hepatic dysfunction
- **Symptoms**: impaired memory and motor function, **asterixis ("flapping tremor")**, personality changes, coma
- Categorized with West Haven criteria (WHC grades 1 to 4)
- Diagnosed by excluding other causes of cognitive dysfunction
- **Short-term** protein restriction may be necessary for nitrogen modulation

- Treatment recommended for fully symptomatic overt HE
 - **Lactulose** (nonabsorbable disaccharide): preferred treatment
 - 30-45 mL every 1-2 hours until at least 2 soft stools/day are produced
 - Thereafter, titrated to maintain 2-3 soft stools/day
 - **Rifaximin** (add-on to lactulose) to **prevent** HE recurrence after **second** episode
 - 550 mg twice daily

Reference:

[1] American Association for the Study of Liver Diseases; European Association for the Study of the Liver. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases. J Hepatol. 2014 Sep;61(3):642-59. doi: 10.1016/j.jhep.2014.05.042. Epub 2014 Jul 8. Erratum in: J Hepatol. 2015 Oct;63(4):1055.

[2] Biggins SW, Angeli P, et al. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 Practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021 Aug;74(2):1014-1048. doi: 10.1002/hep.31884.

[3] Garcia-Tsao G, Abraldes JG, et al. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology. 2017 Jan;65(1):310-335. doi: 10.1002/hep.28906. Epub 2016 Dec 1. Erratum in: Hepatology. 2017 Jul;66(1):304.

[4] Smith A, Baumgartner K, et al. Cirrhosis: Diagnosis and management. Am Fam Physician. 2019;100(12):759-770.

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